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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,722	12/10/2004	Peter Neu	00143-00244-US	6059

23416 7590 04/02/2009
CONNOLLY BOVE LODGE & HUTZ, LLP
P O BOX 2207
WILMINGTON, DE 19899

EXAMINER	
ARNOLD, ERNST V	

ART UNIT	PAPER NUMBER
1616	

MAIL DATE	DELIVERY MODE
04/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,722	NEU ET AL.	
	Examiner	Art Unit	
	ERNST V. ARNOLD	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,7,8 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4,7,8 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 3, 4, 7, 8, and 18 are pending and under examination.

Applicant has amended the claims by limiting the patient population to those with coronary vasospasm and bronchial spasms which were not previously presented and necessitated a new ground of rejection. Accordingly, this Action is FINAL.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 3, 4, 7, 8 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Petzelt et al. (WO 00/53192) in view of Thomas (US 6,358,536) and Zapol et al. (US 6,656,452) and Briend et al. (US 5670177) as evidenced by Giller et al. (Abstract: Am J Neuroradiol 1990, 11(1), 177-82) and Del Ben et al. (Lancet, 2001, 358, page 1369) and O'Rourke et al. (Abstract: Am Rev Respir Dis 1992, 146(5 Pt 2), S11-4).

Applicant claims a method of treating a patient characterized in that a xenon spasmolytic is provided in a form of a combination medicament comprising xenon selected from the group consisting of gaseous xenon and a xenon containing gas mixture, and a further spasmolytic, administering the xenon to a patient in a subanesthetic amount wherein the xenon containing gas mixture administered to the patient contains no more than 60% by volume of xenon and when the xenon containing gas mixture is metered into the patient's respiratory gas the combined gas supplied to the patient contains from 5 to 60% by volume xenon, administering the further spasmolytic orally or intravenously, and the combination medicament is administered to a patient as a medicament for a treatment of spasms, and selecting as a patient some one suffering from coronary vasospasms or bronchial spasms, and wherein the xenon is used with the intended purpose of acting as an effective coronary or bronchial spasmolytic.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Petzelt et al. disclose preparations and methods of use of xenon or xenon gas mixtures for treating neurointoxications (a chronic cerebral disorder such as Parkinson's disease; thus an impairment of cognitive performance) in a therapeutically useful concentration (Page 5, paragraph 1; page 11, paragraph 4 and claims 1, 7 and 16, for example). Petzelt et al. teach the use of the gas or gas mixtures where the neurointoxication is craniocerebral trauma (claims 1-3 and 8). Petzelt et al. clearly point towards a method of treating apoplexy and reducing the damage occurring from apoplexy thus encompassing stroke (Claim 4 and page 7, first paragraph). Petzelt et al. clearly direct one to treat ischemia or craniocerebral tauma with the gas mixture over several hours to one day (page 8, second paragraph). The preparation can have a

ratio of xenon to oxygen of 80 to 20 percent by volume (Page 8, second paragraph and claims 15 and 17). Administration is by simple inhalation (Page 12, line 1). Methods of mixing the gases are provided (Page 8, paragraphs 3 and 4). Methods of administration are also provided (Page 9, paragraphs 1 and 2). Petzelt et al. teach a method of producing an inhalable preparation by mixing xenon with another gas harmless for humans (Claim 18).

Thomas teaches methods of alleviating or preventing vasoconstriction, coronary artery obstruction or vasospasm in a mammal via administration of a NO source (Abstract). The NO source can be nitroglycerine, arginine and a nitroprusside salt (claims 1-37).

Zapol et al. teach use of a therapeutically effective amount of inhaled NO gas for treating ischemia reperfusion, stroke and trauma; for example (Abstract, column 2, lines 50-55 and claim 1). Zapol et al. teach administering a therapeutically effective amount of a second compound that potentiates the therapeutic effect of gaseous nitric oxide (Claim 1). Nitric oxide is a known vasodilator (column 1, lines 22-40).

Briend et al. teach methods of treating ischemia and embolism with intravascular administration of a gaseous mixture of an effective amount of nitric oxide and xenon (claims 1-12; and column 4, lines 31-34).

Giller et al. teach xenon as a cerebral vasodilator (abstract).

Del Ben et al. teach that coronary vasospasm is induced by increased norepinephrine release (left column top).

O'Rourke et al. teach that norepinephrine contracts smooth muscle for control of bronchial vascular tone (Abstract). Therefore, norepinephrine is known as a vasoconstrictor.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Petzelt et al. do not expressly teach a method of treating spasms such as cerebral vasospasm in a patient with xenon and a spasmolytic wherein xenon is used with the intended purpose of acting as an effective spasmolytic. This deficiency in Petzelt et al. is cured by the teachings of Zapol et al., and Thomas and Briend et al. as evidenced by Giller et al., Del Ben et al., and O'Rourke et al.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use an NO source as defined by Zapol et al. or Thomas, in the method of Petzelt et al., for the treatment of coronary vasospasms or bronchial spasms wherein xenon is used with the intended purpose of acting as an effective spasmolytic and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Petzelt et al. teaches in claims 1-3:

1. Use of xenon or xenon gas mixtures for treating neurointoxications.

2. Use according to claim 1, characterized in that the neurointoxication is caused by a neurotransmitter excess.

3. Use according to claim 1 or 2, characterized in that the xenon reduces the release of dopamine, glutamate and/or noradrenalin.

Noradrenalin is another name for norepinephrine and norepinephrine is taught in the art by O'Rourke et al. and Del Ben et al. to be responsible for bronchial and coronary contraction/vasoconstriction. Thus, the instantly claimed pathological states fall under the teachings of Petzelt et al. as having excess neurotransmitter present causing the conditions and the neurotransmitter is norepinephrine which is taught by Petzelt et al. as noradrenalin. Furthermore, Petzelt et al. suggests adding another harmless gas, and a therapeutic amount of NO from an NO source would be beneficial to the patient as taught by Zapol et al., Briend et al., and Thomas. With regard to the limitation of "wherein xenon is used with the intended purpose of acting as an effective spasmolytic", it is the Examiner's position that Petzelt et al. would have known that xenon was a vasodilator and hence "spasmolytic" because of the teachings of Giller et al. Since the methods of Petzelt et al. and Thomas and Zapol et al. are directed to the same purpose it would be obvious to combine xenon and NO especially in view of the fact that Petzelt et al. suggests other gases and Thomas and Zapol et al. teach using NO sources for treating the same conditions. One of ordinary skill in the art would have combined the two compositions, xenon and NO source, in the method of Petzelt et al. It is the Examiner's position that mixing of xenon and NO gases would read on simultaneous administration and that it is within the purview

of one of ordinary skill in the art to determine the best mode of administration on a patient by patient and condition dependent manner where separate or sequential administration might be most favorable for that case.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

One of ordinary skill in the art would have recognized the obvious variation of the instant claims in the copending application because of the overlap in claimed subject matter as stated above.

Response to arguments:

Applicant asserts that: "Petzelt is completely silent about any advantageous effect of xenon when using it as a gas mixture in combination with further spasmolytic as an effective therapeutic agent for the treatment of bronchial spasms and coronary vasospasms." Respectfully, the Examiner cannot agree with this statement. Petzelt has broadly claimed conditions where an excess of neurotransmitter is present. In the case of spasms/constrictions, excess norepinephrine,

a neurotransmitter, is responsible for the condition. Therefore, coronary vasospasm and bronchial spasms reasonably fall within the scope of the teachings of Petzelt. The next question is whether or not it is known to administer nitric oxide to treat spasms. The answer is yes as taught by the cited art above. Thomas, for example, broadly teaches treating vasoconstriction and vasospasm in a mammal which would include coronary vasospasm and bronchial spasms/constrictions. Respectfully, the combination of two medicaments taught for the same purpose is obvious to one of ordinary skill in the art in the absence of evidence to the contrary.

Respectfully, Applicant's arguments are not persuasive in view of the new ground of rejection.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F (6:15 am-3:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Ernst V Arnold/
Examiner, Art Unit 1616